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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,336	03/22/2001	Mangus Von Knebel-Doeberitz	4121-121	7154

7590 01/17/2002

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1633	6

DATE MAILED: 01/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,336	VON KNEBEL-DOEBERITZ ET AL.	
	Examiner	Art Unit	
	Celine Qian	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☒ Claim(s) 9 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-9 are pending in the application.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany 198 25 620.5 on 06/08/1998. It is noted, however, that applicant has not filed a certified copy of the 198 25 620.5 application as required by 35 U.S.C. 119(b), and therefore has not perfected the claim for foreign priority. Accordingly, the effective filing date is 12/08/2000.

Specification

The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to the drawings, each of the lettered items should appear in upper case, without underling or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-Reference to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Sequence Listing," a table, or a computer program listing appendix submitted on compact disc (see 37 CFR 1.52(e)(5)).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(i) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing, if on paper (see 37 CFR 1.821-1.825).

The specification is objected to because of a number of informalities listed below:

1) It lacks appropriate headings as shown above. 2) There are no page numbers in the specification. 3) The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. Applicants are required to submit a new copy of specification with appropriate heading inserted and written with lines double-spaced on good quality paper.

The specification is further objected to because the description of Figure 2a+b is not clear. The description refers to gray columns in figure whereas there are only black columns in figure. The specification is further objected to because the columns and rows in Table 1 do not have any proper headings. The specification is further objected to for using terminology not consistent with which is accepted by art. Applicants use "naked mouse" throughout the specification. However, it appears that applicants mean "nude mouse" which has a particular phenotype. It is not clear whether "naked mouse" has the same phenotype or just some mouse without hair or clothing. It is advised that applicants use terminology that is generally accepted by art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention is a method of using adeno-associated viruses for lowering the radiotherapy-induced or chemotherapy-induced resistance in patients who suffer from a cancer and a pharmaceutical composition containing a chemotherapeutic agent and adeno-associated viruses. The specification discloses that adeno-associated virus AAV2 sensitizes small cell lung cancer cell lines to chemotherapeutic agent cisplatin and etoposide (see example 1). The specification further discloses that AAV2 sensitizes tumor cells to cisplatin and etoposide in nude mice (see example 3).

As early as in 1992, Walz et al. demonstrated that AAV2, a non-pathogenic virus, sensitizes HeLa cells to gamma radiation. In 1996, Klein-Bauernschmitt et al. showed that AAV2 also sensitizes a number of tumor cell lines, including cervical cacinoma cell line, glioblastoma cell line, melanoblastoma cell line and breast carcinoma cell line, to chemotherapeutic agents both in vitro and in nude mouse. However, until present, there is no report that AAV2 is able to lower radiotherapy-induced or chemotherapy-induced resistance in patients who suffer from a cancer. It is also well known in the art that the molecular basis of cancer varies from every type of cancer and there is no single agent that works for all types of cancer. The success in cell lines and (nude) mouse studies are not predictive of outcomes in cancer patients.

The amount of direction or guidance presented in the specification is limited. Applicant only discloses that small cell lung cancer cell lines and cancer cells induced by said cell lines in nude mice are sensitized to chemotherapeutic agents with concomitant AAV2 infection. Applicants have not provided guidance in the specification toward specific treatment protocols or a pharmaceutical composition containing a chemotherapeutic agent and AAV2 that would show

AAV2 infection is capable to reduced radiotherapy or chemotherapy-induced tumor resistance in patients.

The breath of the claims is very broad. The broadest claim is especially so because it is drawn to a method of using any adeno-associated viruses for lowering the radiotherapy-induced or chemotherapy-induced resistance in patients with cancer. In addition, the claims are also drawn to a pharmaceutical composition containing a chemotherapeutic agent and adeno-associated viruses. However, the specification fails to disclose a working example for a method to treat cancer patients with a combination of a chemotherapeutic agent and an AAV2. The specification also fails to disclose a composition comprising such a combination with therapeutic effect in cancer patients. Without guidance from the specification or the prior art, empirical experimentation would be required to determine a number of issues including (1) whether AAV2 infection is capable to sensitize tumors in patients to chemo or radiotherapy induced resistance, (2) the effective amount to achieve said sensitization, and (3) whether it is safe to use AAV2 for patients. Without guidance from the prior art and the specification, one skilled in the art would require undue amount of experimentation to practice the method that is claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 provide for the use of adeno-associated viruses, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J Clark can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
January 14, 2002

REMY YUCEL, PH.D
PRIMARY EXAMINER